Serial Measurement of Biomarkers of Rhabdomyolysis to Assess Severity of Muscle Damage in Tibial Fractures – A Prospective Multicenter Cohort Study

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INTRODUCTION: Trauma-related muscle damage likely occurs to some degree in all tibial fractures. Acute compartment syndrome (ACS) is a devasting complication of injury that causes additional muscle injury and eventual myonecrosis. Since both the injury and ACS share overlapping symptoms, accurate diagnosis of ACS is challenging. Distinguishing between these conditions is crucial for effective clinical decision-making when ACS is emerging. Our study investigates the time-course of myoglobin (P-Myo) and creatine kinase (P-CK) levels in patients with tibial fractures who did not have ACS. We hypothesized that patients with high-energy or multitrauma fractures would exhibit higher P-Myo and P-CK values compared to those with low-energy or isolated tibial fractures.

METHODS: We conducted a prospective, multicenter cohort study involving patients aged 15–65 years with tibial fractures across five hospitals in Sweden and Finland from 2018 to 2021. Exclusion criteria included malignancy, acute myocardial infarction, renal insufficiency (GFR ≤ 35 mL/min), muscle disease, and paraplegia/tetraplegia. We analyzed P-Myo and P-CK levels at 6-hour intervals for 48 hours post-trauma. Using a multiple linear regression model, we explored differences in biomarker levels based on predefined patient and injury characteristics. The time that peak mean values for P-Myo and P-CK occurred following trauma was determined.

RESULTS:

Of the 204 patients included in the study, 27 patients were excluded and 23 had missing values for P-CK and/or P-Myo (Figure 1 and Table 1). Peak mean levels of P-Myo and P-CK were low, 286 (95% confidence interval [CI]: 211 to 362) µg/L and 9.8 (95% CI: 7.1 to 12.5) µkat/L (Figure 2), respectively. Maximum myoglobin values occurred within the first 6 hours after injury, whereas CK levels continued to rise for 18 hours. High energy trauma was associated with higher values for P-Myo, mean difference 472 (95% CI: 302 to 642) µg/L and P-CK, 19 (95% CI: 13 to 25) µkat/L compared to low energy trauma. Multitrauma was associated with higher values for P-Myo, mean difference 1208 (95% CI: 744 to 1672) µg/L and P-CK, 51 (95% CI: 37 to 65) µkat/L compared to isolated tibial fracture. Men had higher P-CK levels compared to women, mean difference 4.8 (95% CI: 0.7 to 8.9) µkat/L. No significant differences were found for age less or above 40 years. High energy trauma yielded higher P-Myo and P-CK, continuously for 48 hours after the injury (Figure 3).

DISCUSSION AND CONCLUSION:

In our study, we investigated the levels of P-Myo and P-CK following tibial fractures. Our findings confirmed our hypothesis that trauma energy is associated with higher levels of both biomarkers. Since peak myoglobin values occurred within the first 6 hours after the injury, myoglobin could serve as an early marker for muscle damage. Further investigation is warranted to determine specific thresholds for myoglobin levels that can rule out ACS. CK levels peaked at up to 18 hours after the injury; this delayed increase may not be practical for assessing muscle damage associated with ACS. Given the urgency of fasciotomy —usually performed within 6–10 hours after onset—myoglobin appears to be a more promising marker. Comparing myoglobin levels between tibial fracture patients with and without ACS could help establish reliable thresholds, allowing clinicians rule out ACS with reasonable confidence and avoid unnecessary fasciotomies.

In summary, our study highlights the potential of myoglobin as an early indicator for ACS, while acknowledging the limitations of CK in this context. To enhance clinical decision-making regarding fasciotomy in tibial fracture cases, further research is necessary to establish specific thresholds for these biomarkers. These thresholds would potentially allow clinicians to confidently rule out ACS and avoid unnecessary fasciotomies.

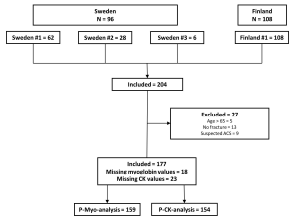

Figure 1. Study flowchart.

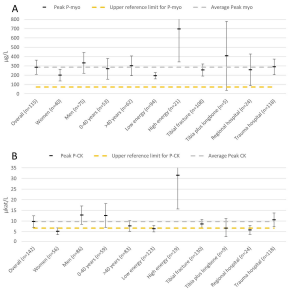

Figure 2: Peak mean values (unadjusted) of P-myo (0–6 hours) (A) and P-CK (0–18 hours) (B) for the different subgroups. Provides upper reference limits are for men. Multitrauma not shown.

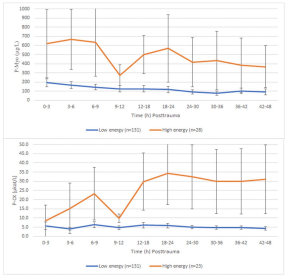

Figure 3: Results from the GEE analysis showing the temporal pattern of P-Myo and P-CK during 48 hours after the trauma stratified for trauma energy.

Patient characteristics n (%)	P-myo (n=159)	P-CK (n=154)
Sex		
Men	96 (60.4)	92 (59.7)
Women	63 (39.6)	62 (40.3)
Age (years), mean (SD)	43 (14)	44 (14)
≤40 years	67 (42.1)	63 (40.9)
>40 years	92 (57.9)	91 (59.1)
Trauma energy		
High energy	28 (18)	23 (14.9)
Low energy	131 (82)	131 (85.1)
Number of fractures		
Tibial fracture	146 (91.8)	141 (91.6)
Tibial and additional long bone fracture	10 (6.3)	10 (6.5)
Multitrauma	3 (1.9)	3 (1.9)
Hospital		
Finland #1	94 (59.1)	94 (61.0)
Sweden #1	40 (25.2)	35 (22.7)
Sweden #2	21 (13.2)	21 (13.6)
Sweden #3	4 (2.5)	4 (2.6)

Table 1. Patient and injury characteristics.